

INTERNATIONAL COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

REC'D 27 SEP 2004



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Applicant's or agent's file reference P10504PC/P10174	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/DK 03/00385	International filing date (day/month/year) 11.06.2003	Priority date (day/month/year) 11.06.2002
International Patent Classification (IPC) or both national classification and IPC G01N15/12		
Applicant CHEMPAQ A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
 - ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 09.01.2004	Date of completion of this report 13.08.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Koch, A Telephone No. +31 70 340-3828 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/DK 03/00385**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-21 as originally filed

Claims, Numbers

1-28 filed with telefax on 02.08.2004

Drawings, Sheets

1/9-9/9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2,3,5,6,8-17,19-22,24,26,28
	No: Claims	1,4,7,18,23,25, 27
Inventive step (IS)	Yes: Claims	2,3,5,6,8-13,19-22,24,26,28
	No: Claims	1,4,7,14,15,16,17,18,23,25,27
Industrial applicability (IA)	Yes: Claims	1-28
	No: Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/DK 03/00385

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D2: US-A-5 231 005 (COULTER WALLACE H ET AL) 27 July 1993 (1993-07-27)
D3: US-B-6 387 3281 (BERNDTSSON INGEMAR) 14 May 2002 (2002-05-14)
D4: WO 93/01306 A (GOUMENIOUK ALEXANDER P ;RICHARDS BRIAN G (CA)) 21 January 1993 (1993-01-21)

1. The closest prior art of amended claim 1 is seen in the document D3 disclosing a cartridge for blood testing.
Regarding claim 1, D3 discloses:
A cartridge for characterizing particles suspended in a liquid sample (col. 1, l. 11-14 of D3),
connectors for operational connection to and disconnection from connectors of a docking station for establishment of electrical and fluid connections when the cartridge is received in the docking station (col. 4, l. 4-15; col. 6, l. 7-22 of D3),
a first mixing chamber (col. 4, l. 57-61),
particle characterization means for characterizing the particles (col. 4, l. 4-15)
a bore in the outer surface of the housing for entrance of the liquid sample (col. 4, l. 24-33, "channel 54"), communicating with
a first sampling member positioned in the housing for sampling the liquid sample and having a first cavity for receiving and holding the liquid sample, the member being movably positioned in relation to the housing in such a way that, in a first position, the first cavity is in communication with the bore for entrance of the liquid sample into the first cavity, and, in a second position, the first cavity is in communication with the first mixing member for discharge of the liquid sample into the first mixing chamber whereby the sampling member operates to receive and hold a precise volume of liquid sample and to transfer the sample to the first mixing chamber (col. 3, l. 49-67; col. 4, l. 36-41),
characterized in that the cartridge further comprises
a first collection chamber separated by a wall from the first mixing chamber, the wall containing a first orifice for the passage of the particles between the first mixing chamber and the first collection chamber (col. 5, l. 18-24), and in that the first particle characterization means is adapted for characterization of the particles passing through the first orifice (col. 5, l. 18-30).

Therefore claim 1 does not comply with Articles 33(1) and (2) PCT.

2. Independent claim 23 referring to a method of operating a particle characterization apparatus does not comply with the requirements of Articles 33(1) and (2) PCT, since its technical features are also anticipated by the document D3, c.f. the passages cited for claim 1 above.
3. Furthermore, the dependent claims 4, 7, 18, 25 and 27 do not fulfill the requirements of Articles 33(1) and (2) PCT, since all their technical features are also known from the document D3, c.f. the abovementioned passages.
4. Moreover, claims 14, 15, 16 and 17 do not meet the requirements of Articles 33(1) and (3) PCT, the reasons being as follows:
 - 4.1 D4 which describes a diagnostic kit and methods for making granulocyte cell counts discloses a anti-coagulation reagent and coating the surface of a sampling tube with it (p. 22, l. 19-22 of D4). It would be obvious to the skilled person to apply such a coating also in other blood sampling or storage containers. The technical features of claims 14 and 15 beyond those of the claims to which they refer are therefore known from D4, for the same or a similar technical purpose.
 - 4.2 D2 which discloses a method and apparatus for automatic analysis and counting of different types of blood cells describes the use of a magnetic mixing member in a mixing chamber (col. 7, l. 64-col. 8, l. 6; col. 10, l. 33-36 of D2). It would be obvious to the skilled person to apply a magnetic mixing member also in the mixing chamber mentioned in the application.
5. The technical features of claims 2, 3, 5, 6, 8-13, 19-22, 24, 26 and 28 which these claims comprise beyond those of the claims to which they refer are not known from any of the prior art documents and thus seem to be suitable to distinguish the method and apparatus of the application from the prior art methods and devices (Articles 33(1)-(3)).

CLAIMS

1. A cartridge for characterizing particles suspended in a liquid sample, comprising a housing with
 - connectors for operational connection to and disconnection from corresponding
 - 5 connectors of a docking station for establishment of electrical and fluid connections when the cartridge is received in the docking station,
 - a first mixing chamber,
 - first particle characterization means for characterizing the particles ,
 - a bore in the outer surface of the housing for entrance of the liquid sample,
 - 10 communicating with
 - a first sampling member positioned in the housing for sampling the liquid sample and having a first cavity for receiving and holding the liquid sample, the member being movably positioned in relation to the housing in such a way that, in a first position, the first cavity is in communication with the bore for entrance of the liquid sample into the
 - 15 first cavity, and, in a second position, the first cavity is in communication with the first mixing chamber for discharge of the liquid sample into the first mixing chamber whereby the sampling member operates to receive and hold a precise volume of liquid sample and to transfer the sample to the first mixing chamber
 - c h a r a c t e r i z e d in that the cartridge further comprises
 - 20 a first collection chamber separated by a wall from the first mixing chamber, the wall containing a first orifice for the passage of the particles between the first mixing chamber and the first collection chamber, and in that
 - the first particle characterization means is adapted for characterization of the particles passing through the first orifice.
- 25 2. A cartridge according to claim 1, further comprising
 - a second mixing chamber and a second collection chamber separated by a second wall containing a second orifice for the passage of the particles between the second mixing chamber and the second collection chamber,
 - second particle characterization means for characterizing particles passing through the
 - 30 second orifice, and wherein
 - in the second position, the first cavity is in communication with the first mixing chamber for entrance of liquid from the first mixing chamber into the first cavity, and, in a third

position, the first cavity is in communication with the second mixing chamber for discharge of the liquid in the first cavity into the second mixing chamber.

3. A cartridge according to claim 1, further comprising

a second mixing chamber and a second collection chamber separated by a second wall containing a second orifice for the passage of the particles between the second
5 mixing chamber and the second collection chamber,

second particle characterization means for characterizing particles passing through the second orifice, and

a second sampling member positioned in the housing for sampling a small and precise
10 volume of liquid from the first mixing chamber and having a second cavity for receiving and holding the sampled liquid, the member being movably positioned in relation to the housing in such a way that, in a first position, the second cavity is in communication with the first mixing chamber for entrance of liquid from the first mixing chamber into the first cavity, and, in a second position, the second cavity is in communication with
15 the second mixing chamber for discharge of the sampled liquid in the second cavity into the second mixing chamber.

4. A cartridge according to any of the preceding claims, further comprising a reagent chamber positioned adjacent to the first mixing chamber for holding a reagent to be entered into the first mixing chamber.

20 5. A cartridge according to claim 4, further comprising a breakable seal separating the reagent chamber from the first mixing chamber.

6. A cartridge according to any of the preceding claims, wherein at least one of the first and second particle characterization means includes a first electrode in the respective one of the first and second mixing chamber and a second electrode in the
25 respective one of the first and second collection chamber, each electrode being electrically connected to a respective terminal member accessible at the outer surface of the cartridge.

7. A cartridge according to any of the preceding claims, wherein the housing further comprises a first liquid storage chamber for holding a liquid and that, in the second
30 position of the first sampling member, communicates with the first cavity so that liquid can be discharged from the first liquid storage chamber through the first cavity of the first sampling member and into the first mixing chamber together with the liquid sample.

8. A cartridge according to any of the preceding claims, wherein the housing further comprises a second liquid storage chamber for holding a liquid to be discharged from the second liquid storage chamber through the respective one of the first and second cavity and into the second mixing chamber together with the sampled liquid.
- 5 9. A cartridge according to any of the preceding claims, comprising volume metering means for determining the beginning and end of a period during which a predetermined volume of liquid has passed through at least one of the first and second orifice.
10. A cartridge according to claim 9, wherein the volume metering means comprises a volume metering chamber with an input communicating with the respective collection chamber and an output, and wherein presence of liquid is detected at the input and at the output, respectively.
11. A cartridge according to claim 10, wherein presence of liquid is detected with a secondary electrode positioned at the input and a further secondary electrode positioned at the output.
- 12 12. A cartridge according to claim 10, wherein presence of liquid is detected optically.
13. A cartridge according to any of the preceding claims, wherein each of the mixing chambers and the collection chambers has a transverse cross-sectional area at the level of the respective orifice which is substantially less than the transverse cross-sectional area of the respective chamber over a substantial part of the height of the chamber above the respective orifice.
- 20 14. A cartridge according to any of the preceding claims, wherein the surface defining the first cavity of the first sampling member has an anti-coagulation reagent.
15. A cartridge according to any of the preceding claims, wherein the first liquid storage chamber holds chemical reagents for modification of the blood sample.
- 25 16. A cartridge according to any of the preceding claims, wherein a mixing member is positioned in at least one of the mixing chambers.
17. A cartridge according to claim 16, wherein the mixing member is magnetic.
18. A cartridge according to any of the preceding claims, further comprising a sensor for characterization of the liquid.
- 30 19. A cartridge according to claim 18, wherein the sensor for characterization of the liquid is adapted for spectrophotometric characterization of the liquid.

20. A cartridge according to any of the preceding claims, wherein the housing further comprises a pump chamber communicating with one of the first and second collection chambers and having a pump actuator for causing a liquid flow through the respective orifice.

5 21. A cartridge according to claim 20, wherein the pump actuator is a piston.

22. A cartridge according to claim 20, wherein the pump actuator is a membrane.

23. A method of operating a particle characterization apparatus comprising a cartridge according to any of the preceding claims, the cartridge being demountable from the apparatus, the method comprising

10 sampling liquid containing particles with the cartridge through the bore with the first sampling member in its first position,

positioning the cartridge in the apparatus,

moving the first sampling member to its second position,

pumping liquid in the first storage chamber through the second cavity and into the first

15 mixing chamber together with the liquid sample,

making particle characterizing measurements,

disconnecting the cartridge from the apparatus, and

discarding the cartridge.

20 24. A method of operating a particle characterization apparatus comprising a cartridge according to claim 3 or any of claims 4-22 as dependent on claim 3, the cartridge being demountable from the apparatus, the method comprising

sampling liquid containing particles with the cartridge through the bore with the first sampling member in its first position,

positioning the cartridge in the apparatus,

25 moving the first sampling member to its second position,

pumping liquid in the first storage chamber through the first cavity and into the first mixing chamber together with the liquid sample,

sampling a liquid sample from the first mixing chamber with the second sampling member in its first position,

30 moving the second sampling member to its second position,

pumping liquid in the second storage chamber through the second cavity and into the second mixing chamber together with the liquid sample,

making particle characterizing measurements,

disconnecting the cartridge from the apparatus, and

5 discarding the cartridge.

25. An apparatus for characterizing particles suspended in a liquid, comprising a cartridge according to any of claims 1-22, and

a docking station for removably receiving the cartridge, comprising connectors for operational connection with the particle characterization means when the cartridge is
10 received in the docking station.

26. An apparatus according to claim 25, wherein

the cartridge further comprises a first port communicating with the first collection chamber for causing a liquid flow through the first orifice, and

15 the docking station further comprises a port for forming a gas connection with the with the cartridge port when the cartridge is received in the docking station for application of a pressure causing a liquid flow through the orifice.

27. An apparatus according to claim 25 or 26, comprising a cartridge according to any of claims 2-24, the docking station further comprising connectors for operational connection with the second particle characterization means when the cartridge is
20 received in the docking station.

28. An apparatus according to claim 27, wherein

the cartridge further comprises a second port communicating with the second collection chamber for causing a liquid flow through the second orifice, and

25 the docking station further comprises a second port for forming a gas connection with the with the second cartridge port when the cartridge is received in the docking station for application of a pressure causing a liquid flow through the second orifice.